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PATHOGENESIS OF CAKUT SYNDROME AND THE EASIEST WAYS TO INSTILL STUDENTS IN THE COURSE OF THE LESSON

Annotation: The abbreviation CAKUT stands for the term "congenital anomalies kidney and urinary tract", which in the Russian interpretation sounds like " congenital anomalies of the kidneys and urinary tract (VAPMP)". The frequency of occurrence of the syndrome is from 3 to 6 cases per 1000 newborns. It causes more than 50% of cases of chronic kidney disease(CKD), so it is of great importance in pediatric nephrology. The disease is equally common in children of both sexes. Significant ethnic and geographical features of its distribution were not found.

Key words: CAKUT syndrome , genetic mutations, blood vassels, external influences

Like other congenital malformations in children, anomalies of the kidneys and lower urinary tract have a multifactorial nature and an insufficiently studied etiology. The type and time of exposure to the provoking factor determines exactly what developmental disorders will occur in a particular patient and how much the urinary function will suffer in the postnatal period. Main causes of CAKUT syndrome:

- Genetic mutations. The development of the disease is associated with abnormalities of the PAX2 and HNF1B genes, which play a crucial role in the embryonic formation and differentiation of renal tissue and urinary tract structures. If the pathology is accompanied by damage to other organs and systems, this form of the disease is called CAKUT syndrome.
- External influences. The likelihood of kidney abnormalities increases if a pregnant woman takes nephrotoxic drugs, has a deficiency of folic acid and iron. An independent risk factor for CAKUT syndrome is maternal diabetes mellitus, including gestational disorders of carbohydrate metabolism that were not diagnosed in time.

The hereditary nature of the pathology is determined in children in 10-20% of cases. In general, the transmission of genes responsible for the development of urological abnormalities occurs by an autosomal dominant mechanism. It is enough for an infant to have a copy of the mutant gene from one of the parents to develop characteristic mutations. In rare cases, an autosomal recessive inheritance pathway is determined, when for the formation of CAKUT syndrome it is necessary to obtain one abnormal gene from each of the parents.

Pathogenesis

The disease includes various congenital malformations that range from asymptomatic abnormalities to critical organ structure disorders. Kidney damage is represented by agenesis – the absence of an organ, hypoplasia – underdevelopment of the parenchyma, anomalies in shape, size and location. Polycystic kidney disease is often diagnosed. Urinary tract abnormalities include doubling of the ureters, megaureter, vesicoureteral fistula stenosis, and posterior urethral valves.

The nature and severity of malformations depends on the time of pathological exposure and correlates with the peculiarities of embryogenesis of the urinary system. The formation of a secondary "adult" kidney (metanephros) in children begins at the 2nd month of intrauterine development, by the end of the 12th week of gestation, the organ begins to function. The bladder and urethra are formed at 4-8 weeks of the antenatal period of life.

Disorders of embryogenesis at 4-7 weeks of gestation cause severe variants of CAKUT syndrome, since teratogenic factors lead to the complete absence of organs or their significant structural changes. This condition is more often associated with genetic abnormalities. Exogenous influences in the second half of intrauterine development cause minor structural or functional disorders in the kidneys and urinary system.

The time of occurrence and intensity of clinical signs of CAKUT syndrome depends on the type of pathology Unilateral non-critical damage to the urinary organs does not manifest itself for a long time, being detected only with the development of complications. Symptoms of gross abnormalities of the kidneys (agenesis) and lower urinary structures occur in the first weeks after birth.
Many babies with CAKUT syndrome are born prematurely, have low body weight, visible deformities of the skeleton and face. Children have a painful appearance, pathological pallor of the skin, constant lethargy and drowsiness. The increase in intoxication causes polymorphic neurological manifestations up to loss of consciousness and coma. It is also characterized by a decrease in the volume and frequency of urination.
The addition of infection against the background of abnormalities of the excretory system causes pyelonephritis, which is manifested by high fever, weakness, repeated regurgitation and vomiting. The urine becomes cloudy and gets a sharp unpleasant smell. Infectious syndrome in children is supplemented by a sluggish sucking reflex, refusal of breast, in older age – lack of appetite, complaints of nausea and headaches.

Complications

Combined damage to different parts of the urinary system in children is more severe than isolated anomalies of one organ. In 48-59% of cases, CAKUT syndrome causes chronic renal failure already in childhood. Over time, 34-43% of patients develop terminal forms of kidney disease that require replacement therapy, are combined with impaired immune function, hemodynamics, and hematopoiesis.
The complex of CAKUT anomalies is observed in more than 500 different hereditary syndromes that affect the urinary, cardiovascular, digestive and nervous systems. The syndromic form of the disease is characterized by a severe course, the appearance of signs immediately after birth, and the rapid development of multiple organ failure. Often, such children die in the neonatal or infancy period.

Diagnostics

Due to the improvement of ultrasound diagnostics, prenatal detection of many malformations during routine ultrasound screenings has become possible. Early detection of signs of CAKUT syndrome is necessary for choosing the tactics of prolonging pregnancy and emergency care for the child in the neonatal period. After birth, patients undergo a comprehensive examination using the following methods::

- Ultrasound of the urinary system. Sonography can detect changes in the location, size, and structure of the renal parenchyma. Also, the expansion of the ureter and the deformation of the bladder are well visualized. The study is supplemented by ultrasound Dopplerography of the renal vessels to diagnose concomitant abnormalities of the arteries and veins.
- Excretory urography. X-ray imaging with contrast provides valuable information about the structure of the calico-pelvic system and all parts of the urinary tract. Functional activity of the renal parenchyma and ureteral patency are evaluated by the features of the distribution and rate of contrast agent advance.
- Renoscintigraphy. Radionuclide scanning of the kidneys is recognized as one of the most informative methods for assessing structural changes (static study) and features of the excretory system (dynamic study). Renoscintigraphy is used as a clarifying diagnosis in complex cases.
- CT scan of the kidneys. Computed tomography provides layered images of the kidneys and all urinary tracts, where it is possible to examine in detail the structural changes and determine the nature of the congenital anomaly. MRI scans of the kidneys and pelvic organs are performed to better visualize the walls of the urinary tract and surrounding soft tissues.
- Mycological cystography. Functional diagnostics are prescribed to confirm the reflux of urine from the bladder back to the ureters – one of the most common consequences of CAKUT syndrome. The study is mainly conducted in school-age children who can follow all the doctor's instructions during the procedure.

- Laboratory tests. When making a diagnosis in children, a set of standard methods is required: a clinical blood test, a general urinalysis, a biochemical blood test and measurement of the glomerular filtration rate (GFR). To assess renal function, a Zimnitsky test is prescribed, and urine is backseeded according to indications.

Differential diagnosis

Modern methods of visualization provide a clear image of the structures of the excretory system for the error-free diagnosis of malformations of its development in children. Differentiation of spontaneous anomalies and disorders associated with genetic diseases, such as Meckel-Gruber, Joubert, and short rib syndrome (a complex of Saldino-Noonan, Mayevsky, Verma-Naumov, and Beamer-Langer syndromes), is very difficult. CAKUT with polycystic kidney disease requires exclusion of Bardet-Biedl syndrome.

Treatment of CAKUT syndrome

Surgical treatment

Surgical intervention is the only radical way to correct congenital malformations in CAKUT syndrome. Depending on the nature of the anomaly, an additional or non-functioning kidney is removed, a ureterocyst anastomosis is created, and the renal pelvis is stented. If possible, patients with end-stage CKD undergo nephrotransplantation, which restores urinary function and improves the long-term prognosis.

Conservative therapy

Etiopathogenetic drug treatment is indicated for complications of congenital malformations with acquired diseases: pyelonephritis, lower urinary tract infections, urolithiasis. With progressive GFR reduction in children, renal replacement therapy by hemodialysis or peritoneal dialysis is recommended to avoid uremia and other life-threatening complications.

Since many patients develop chronic kidney disease, much attention is paid to diet and drinking regimen. To minimize edema and the risk of developing hypertension, it is recommended to reduce the intake of table salt, monitor the amount of liquid consumed and the volume of urination. A low-protein diet improves the patient's condition, but is rarely used in pediatrics, so as not to aggravate the delay in physical development.

Prognosis and prevention

The disease is characterized by an unfavorable course, since without treatment, multiple malformations cause critical renal function disorders and early disability in children. The prognosis worsens when CAKUT syndrome is combined with pathologies of other organ systems. Effective primary prevention measures have not been developed due to the wide variety of genetic and teratogenic factors that affect the intrauterine development of urinary organs.

Literature